Remarks

Status of the Claims

The Office Action indicates that claims 1-40 are pending; claims 3, 17-31, and 37-40 are withdrawn; claims 1, 2, 4-16, and 32-36 are rejected; and claim 34 is objected to. In this paper claims 1 and 19 are amended and claims 7, 9-13, 17, 18, 24-26, 30, 31, 33, and 37-40 are canceled.

Amendment to Claims 1 and 19

Claim 1 is amended to recite an HIV Tat antigen; this amendment is supported by original dependent claim 11, which is canceled. A corresponding amendment is made to withdrawn method claim 19.

Objection to Claim 34

Claim 34 is objected to as being a substantial duplicate of claim 33. Claim 33 is canceled. Please withdraw the objection.

Rejections Under 35 U.S.C. § 103(a)

The Office Action maintains two rejections under 35 U.S.C. § 103(a):

- claims 1, 2, 4-10, and 13-16 over Vajdy[1] in view of Keefer;[2] and
- claims 1, 11, and 12 over Vajdy in view of Keefer, Kumar,[3] Haynes,[4] Kang,[5] Tobery,[6] Cease,[7] and Vogel.[8]

Claims 7 and 9-13 are canceled. Applicants respectfully traverse the two rejections of independent claim 1 and the rejection of dependent claims 2, 4-6, and 14-16.

The U.S. Patent and Trademark Office bears the initial burden of establishing a *prima facie* case of obviousness. The *prima facie* case requires three elements:

> First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or

---

[1] Vajdy *et al.*, "Induction of anti-HIV humoral and cell-mediated immune responses by mucosal immunizations using adjuvants and virus-like particles," 7th Conference on Retroviruses and Opportunistic Infections, San Francisco, CA; 7: 95 (abstract no. 108), January 30-February 2, 2000.

[2] Keefer *et al.*, "Studies of High Doses of a Human Immunodeficiency Virus Type 1 Recombinant Glycoprotein 160 Candidate Vaccine in HIV Type 1-Seronegative Humans," *AIDS Research and Human Retroviruses 10*, 1713-23, 1994.

[3] Kumar & Narayan, "Immunization for Long-Term Protection against AIDS Using the Macaque Model," *Virology 285*, 1-5, 2001.

[4] Haynes, "HIV vaccines: where we are and where we are going," *Lancet 348*, 933-37, 1996.

[5] Kang *et al.*, "Development of HIV/AIDS Vaccine Using Chimeric gag-env Virus-Like Particles," *Biol. Chem. 380*, 353-64, March 1999.

[6] Tobery & Siliciano, "Targeting of HIV-1 Antigens for Rapid Intracellular Degradation enhances cytotoxic T Lymphocyte (CTL) Recognition and the Induction of De Novo CTL Responses In Vivo After Immunization," *J. Exp. Med. 185*, 909-20, March 3, 1997.

[7] Cease & Berzofsky, "Toward a Vaccine for AIDS: The Emergence of Immunobiology-Based Vaccine Development," *Ann. Rev. Immunol. 12*, 923-89, 1994.

[8] Vogel, "The Role of Adjuvants in Retroviral Vaccines," *Int. J. Immunopharmacol. 17*, 85-90, 1995.

> references when combined) must teach or suggest all the claim limitations.

M.P.E.P., 8th ed., § 2142. The PTO has not established that any of claims 1, 2, 4-6, or 14-16 is *prima facie* obvious.

Rejection of claims 1, 2, 4-6, and 14-16 over Vajdy in view of Keefer

Independent claim 1 as amended recites three elements: an HIV envelope antigen; a detoxified mutant A subunit of *E.* coli heat labile toxin; and an HIV Tat antigen (previously recited in claim 11). By not including dependent claim 11 in the rejection, the PTO acknowledges that the combination of Vajdy and Keefer does not teach or suggest a composition comprising these three elements.

Rejection of claim 1 over Vajdy in view of Keefer, Kumar, Haynes, Kang, Tobery, Cease, and Vogel

None of the cited secondary references supports the PTO's rejection of claim 1 as *prima facie* obvious. First, none of Vajdy, Keefer, Kumar, Haynes, Kang, Tobery, Vogel, or Cease teaches or suggests including an HIV Tat antigen in a composition in combination with an HIV envelope antigen and a detoxified mutant A subunit of *E. coli* LT.

Second, Cease teaches away from including an HIV Tat antigen in a composition for mucosal immunization against HIV. Both the specification (page 5, lines 8-10) and several of the cited references teach the importance of a cytotoxic T lymphocyte (CTL) response in providing immunity against HIV. For example, Tobery teaches that "a rapid and vigorous $CD8^+$ CTL response, induced by vaccination, can, in principle, prevent disseminated infection in vaccinated individuals who are exposed to the relevant virus." Abstract, page 909. Kang teaches that the hypervariable V3 region of HIV-1 gp120 is an attractive vaccine candidate because it

both "induces the major neutralizing antibodies and stimulates cytotoxic T-lymphocyte response in humans and mice." Kang at page 361, Discussion ¶ 1. And, as the Office Action acknowledges on page 9, Haynes (p. 935) discusses induction of T cell immunity via multivalent mixtures of immunogens "containing sufficient immunogenic CTL and helper epitopes capable of binding to the HLA molecules expressed on antigen-presenting cells . . . ."

Cease teaches that Tat-specific CTL "appear to be rare in the blood of HIV-1-infected humans, and we have so far been unsuccessful in detecting CTL recognition of HIV-1 tat epitopes in any of several strains of mice." Cease at page 942, lines 5-8, internal references omitted. The ordinary artisan, aware of the importance of a CTL response, would not have been motivated to use an HIV Tat antigen in a composition in combination with an HIV envelope antigen and a detoxified mutant A subunit of *E. coli* LT because there would have been no reasonable expectation that the HIV Tat antigen would be a useful immunogen.

Please withdraw the rejections.

Respectfully submitted,

BANNER & WITCOFF, LTD.

/Lisa M. Hemmendinger/

Dated: February 8, 2008

By:_____
Lisa M. Hemmendinger
Registration No. 42,653

Customer No. 22907